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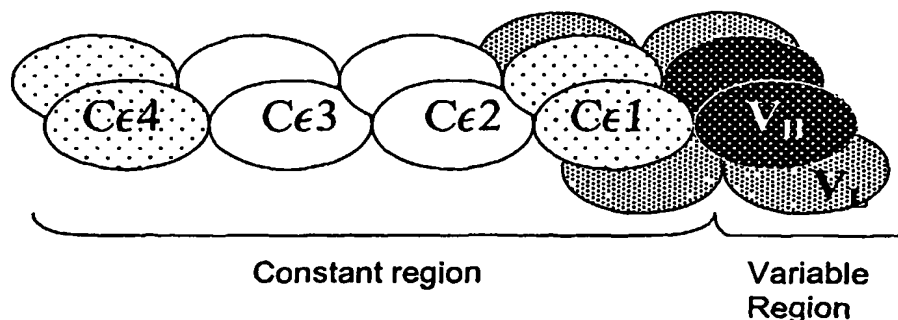
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[Continued on next page]

(54) Title: CAMELIDAE ANTIBODIES AGAINST IMMINOGLOBULIN E AND USE THEREOF FOR THE TREATMENT OF ALLERGIC DISORDERS



(57) Abstract: The invention relates to a method suitable for administering protein therapeutic molecules orally, sublingually, topically, intravenously, subcutaneously, nasally, vaginally, rectally or by inhalation so as to avoid inactivation, by using VHH polypeptides derived from Camelidae antibodies. The invention further relates to the said therapeutic molecules. The invention further a method for delivering therapeutic molecules to the interior of cells. The invention further relates to anti-IgE therapeutic molecules.



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

In tional Application No
PCT/BE 03/00190

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/42 C07K16/24 C07K16/30 C07K16/12 C07K16/10
C07K16/40 C07K16/28 C12N15/13 A61K39/395 A61P11/06
A61P35/00 A61P31/06 A61P31/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, MEDLINE, GENSEQ, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 589 840 A (CIBA GEIGY AG ;TANOX BIOSYSTEMS INC (US)) 30 March 1994 (1994-03-30)	1,6-24, 33,34
Y	page 5, lines 4-16	1-24, 33, 34,58-63
X	US 2002/054878 A1 (LOWE JOHN ET AL) 9 May 2002 (2002-05-09)	1,6-24, 33,34
Y	claims 8-31 examples 2-4	1-24, 33, 34,58-63
X	WO 91/02078 A (PEPTIDE TECHNOLOGY LTD) 21 February 1991 (1991-02-21)	11-25, 59,60,63
Y	page 4, lines 15-24	11-25, 58,61
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

17 June 2004

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Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/BE 03/00190

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	MUYLDERMANS S: "SINGLE DOMAIN CAMEL ANTIBODIES: CURRENT STATUS" REVIEWS IN MOLECULAR BIOTECHNOLOGY, ELSEVIER, AMSTERDAM,, NL, vol. 74, no. 4, June 2001 (2001-06), pages 277-302, XP001057480 ISSN: 1389-0352 table 1	1-24, 33, 34, 58-63
Y	----- VALLE E ET AL: "Infliximab" EXPERT OPINION ON PHARMACOTHERAPY, ASHLEY, LONDON,, GB, vol. 2, June 2001 (2001-06), pages 1015-1025, XP002965315 ISSN: 1465-6566 the whole document -----	11-25

INTERNATIONAL SEARCH REPORT

International application No. —
PCT/BE 03/001 90

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 11-18, 25-39 and 49-57 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
1-24 and 58-63 (in part) and 25-26, 33, 34 (complete)
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 11-18, 25-39 and 49-57 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-24 and 58-63 (in part) and 33, 34 (complete)

A camelidae VHH single domain antibody directed against IgE, in particular, the polypeptides represented by any of SEQ ID NO:1-11; a nucleic acid encoding for said VHH, use of the antibody for the preparation of a medicament for treating or alleviating disorders relating to inflammatory regions, a method for delivering an anti-target compound to a subject by administering the anti-IgE VHH antibodies, the anti-IgE antibodies for use in the treatment of an allergic response, the camelidae VHH anti-IgE which is humanised and the camelidae VHH anti-IgE in a composition together with a pharmaceutical carrier.

2. claims: 11-24 and 58-63 (in part) and 25-26 (complete)

As invention 1 but relating to an anti-TNF-alpha camelidae VHH antibody (SEQ ID NO:12-14) and the uses thereof for the treatment of inflammation.

3. claims: 11-24 and 58-63 (in part) and 27 (complete)

As invention 1 but relating to an anti-CEA camelidae VHH antibody and the uses thereof for the treatment of colon cancer.

4. claims: 11-24 and 49-63 (in part) and 28, 29, 40-44 (complete)

As invention 1 but relating to a single domain antibody directed an internalising cellular receptor, in particular the anti-EGF recetpr camelidae VHH antibody (SEQ ID NO:23-44) and the uses thereof for the treatment of head, neck, lung and colon cancer.

5. claims: 11-24, 39 and 58-63 (in part) and 30 (complete)

As invention 1 but relating to single domain antibodies against an antigen of Helicobacter pylori and the uses thereof for the treatment of indigestion and gastritis.

6. claims: 11-24, 39 and 58-63 (in part) and 31 (complete)

As invention 1 but relating to single domain antibodies against an antigen of Mycobacterium tuberculosis and the uses thereof for the treatment of tuberculosis.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

7. claims: 11-24, 39 and 58-63 (in part) and 32 (complete)

As invention 1 but relating to single domain antibodies against an antigen of the influenza virus and the uses thereof for the treatment of flu.

8. claims: 11-24 and 58-63 (in part) and 35-36 (complete)

As invention 1 but relating to an anti-MMP camelidae VHH antibody (SEQ ID NO:15-22) and the uses thereof for the treatment of cancer.

9. claims: 11-24 and 58-63 (in part) and 37-38 (complete)

As invention 1 but relating to an anti-IFN-gamma camelidae VHH antibody (SEQ ID NO:45-70) and the uses thereof for the treatment of cancer, transplant rejection and an auto immune disorder.

10. claims: 11-24 and 58-63 (in part) and 45, 46 (complete)

As invention 1 but relating to an anti-PDK camelidae VHH antibody and the uses thereof for the treatment of cancer.

11. claims: 11-24 and 58-63 (in part) and 47, 48 (complete)

As invention 1 but relating to single domain antibodies against GSK1, Bad, caspase and Forkhead and the uses thereof for the treatment of cancer.

INTERNATIONAL SEARCH REPORT

Information on patent family members

In tional Application No

PCT/BE 03/00190

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International Application No

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